
بسم الله الرحمن الرحيم
In The Name Of ALLAH
The Most Gracious, The Most Merciful

Armed Forces College of Medicine

AFCM

Male & Female Sex Hormones

Analogs & Inhibitors 1

Prof. / Omayma Khorshid

INTENDED LEARNING OBJECTIVES (ILO)

1.

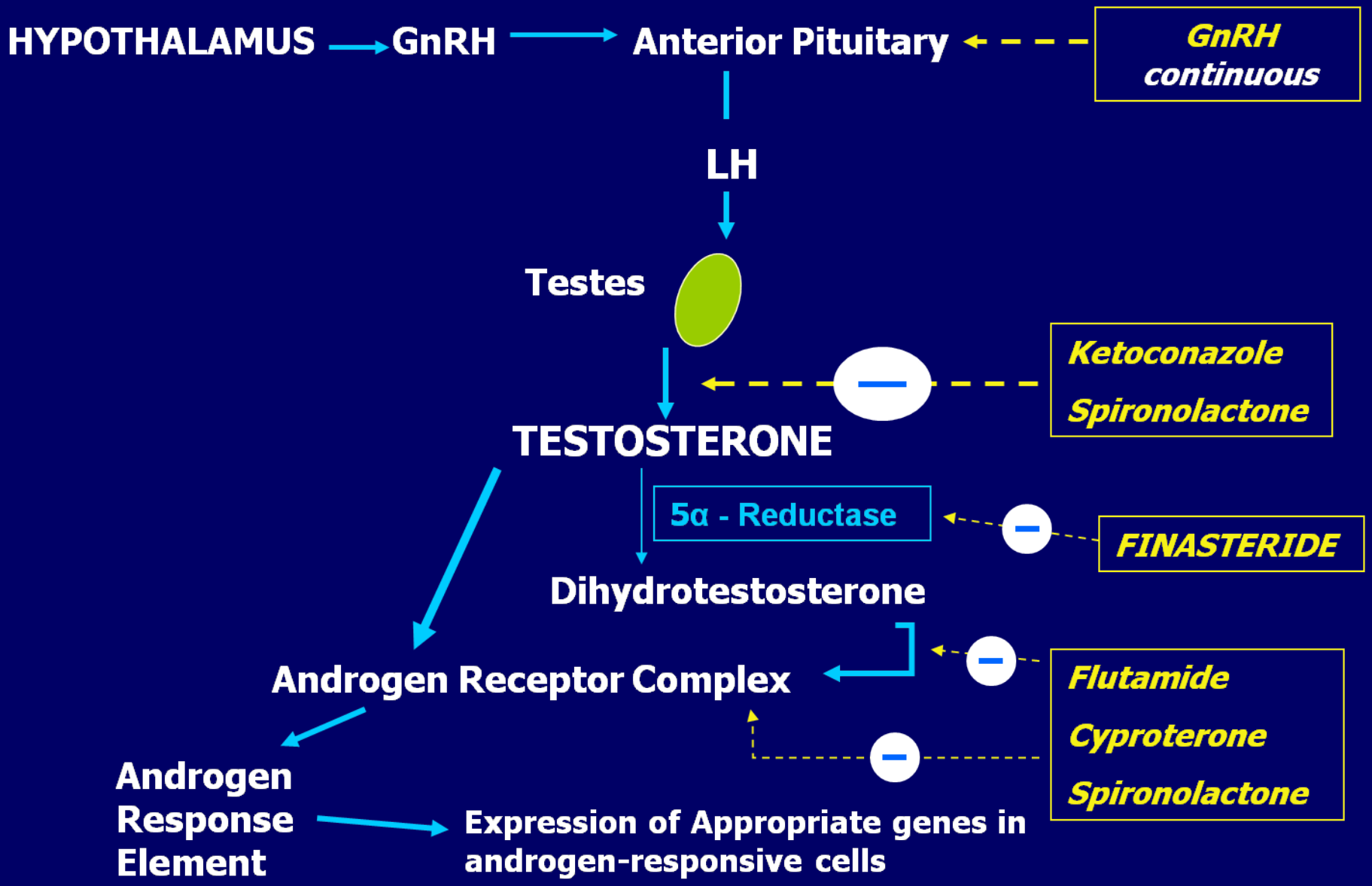
2.

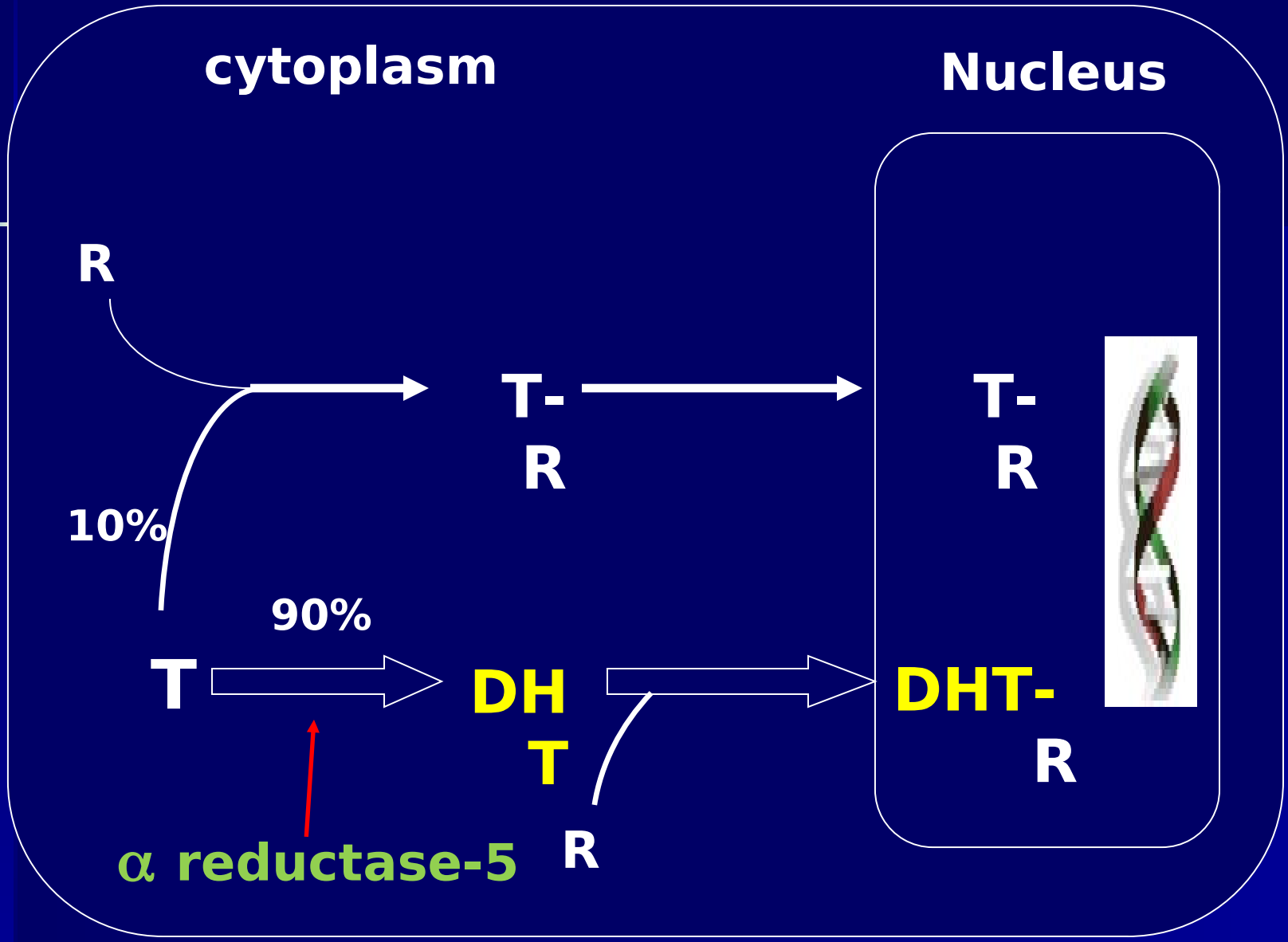
3.

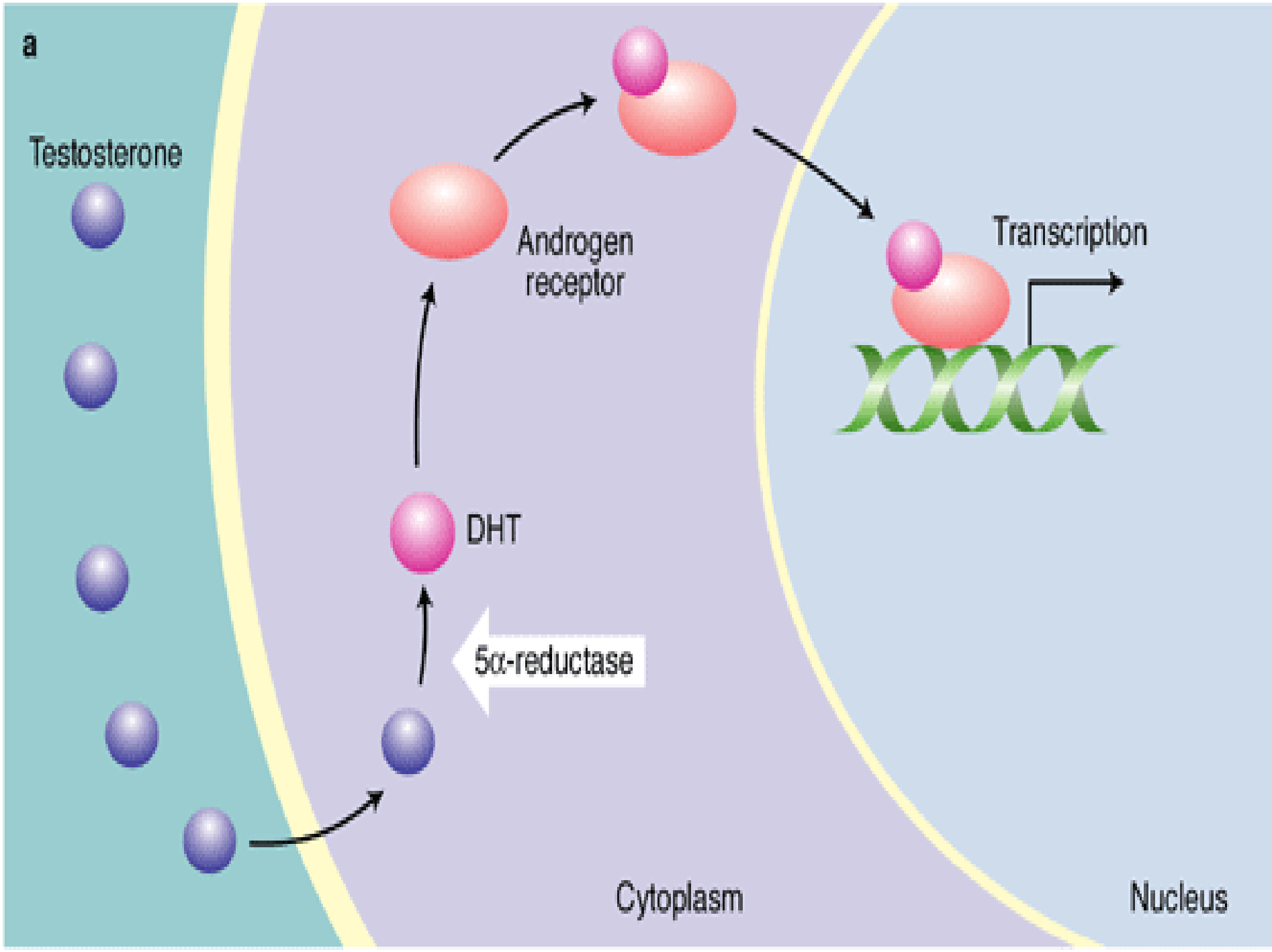
4.

Anti-androgens

Anti-androgens



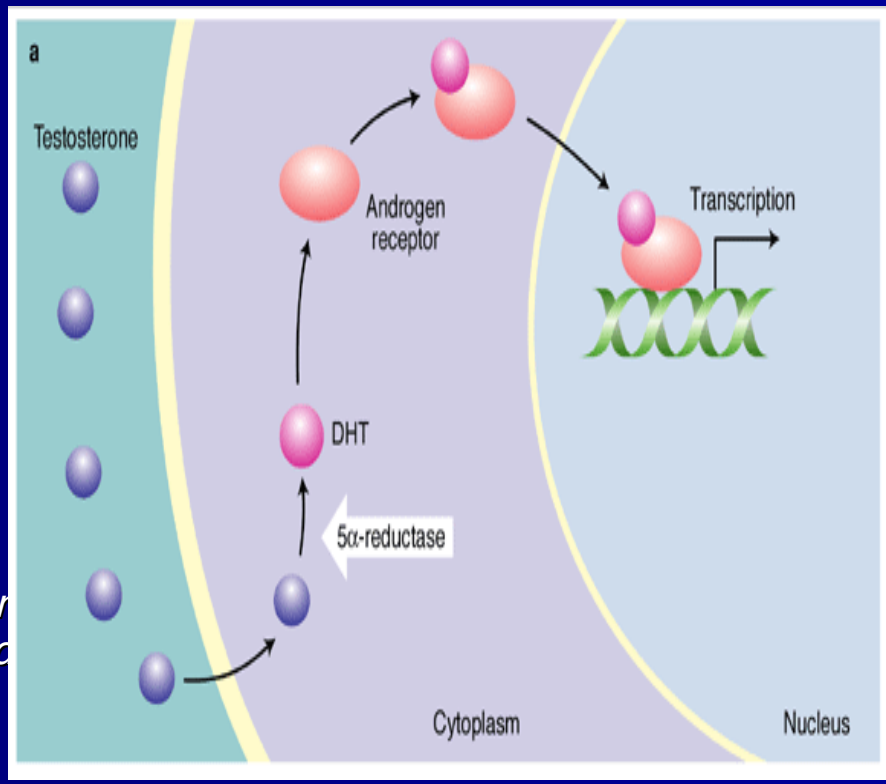

cytoplasm
Nucleus
R
T-
R
10%
90%
T
DH
T
R
α reductase-5
T-
R
DHT-
R


a
Testosterone
Androgen receptor
Transcription
DHT
5α-reductase
Cytoplasm
Nucleus

Finasteride (5α-reductase inhibitor)

- **a steroid-like inhibitor of 5α reductase → ↓ conversion of testosterone to dihydrotestosterone**

N.B: Some tissues, most notably:
prostate cells and hair follicles
depend on DHT Rather than testosterone
for androgenic stimulation.



- **Used for:**

1-benign prostatic hyperplasia

2- hirsutism in females

(lower dose)

Because the drug does not interfere with the actior
antiandrogens to cause impotence, infertility, and

Androgen Recptors Antagonist
Flutamide

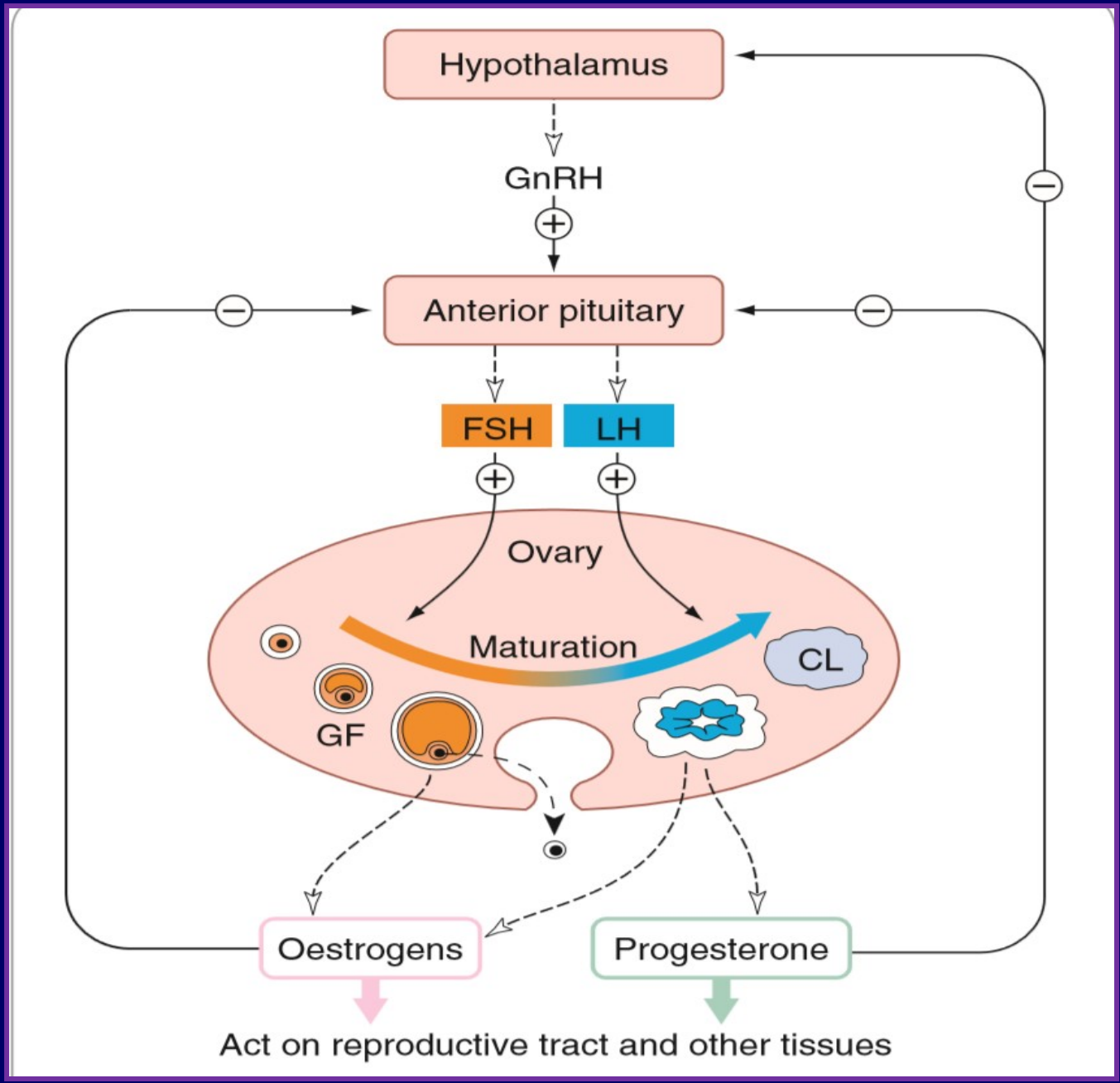
- a nonsteroidal antiandrogen that acts like a competetive antagonist at androgen receptors

- **Used in:**

  Prostatic Ca

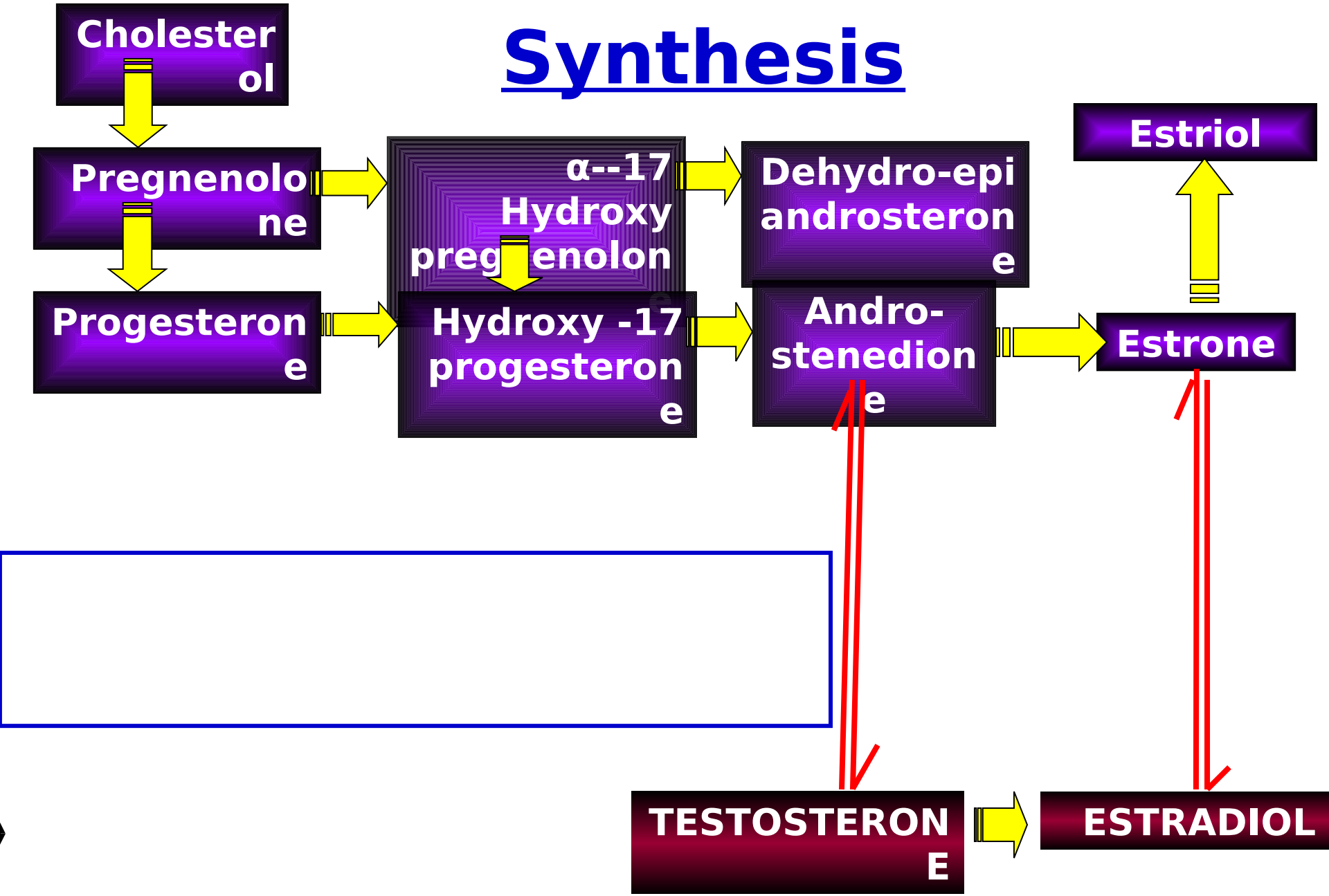
  Hirsutism in females (also spironolactone)

Female Sex Hormones


Hypothalamus
GnRH
Anterior pituitary
FSH
LH
Ovary
Maturation
CL
GF
Oestrogens
Progesterone
Act on reproductive tract and other tissues

Preparations of Estrogens

Synthesis


Cholesterol
Pregnenolone
Progesterone
α--17 Hydroxy pregnenolon
Hydroxy -17 progesterone
Dehydro-epi androsterone
Andro-stenedione
Estriol
Estrone
TESTOSTERONE
ESTRADIOL

Mechanism of Action of estrogen

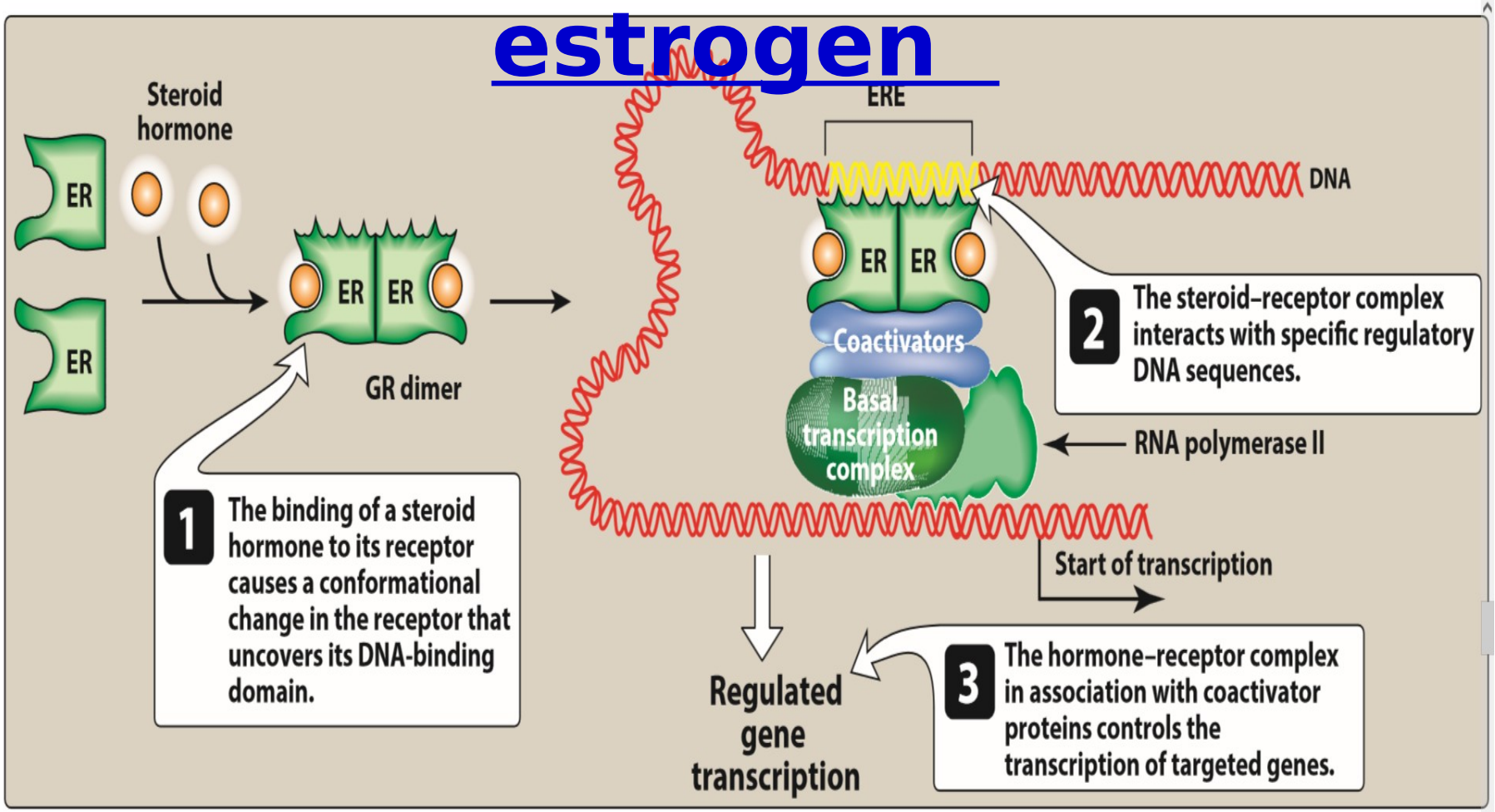


Figure 26.2

Transcriptional regulation by intracellular steroid hormone receptors. ERE = estrogen response element; ER = estrogen receptor.

Mechanism of Action

- Steroid hormones diffuse across the cell membrane and bind with high affinity **to specific nuclear-receptor proteins.**
- The activated **steroid–receptor complex interacts with nuclear chromatin** to **initiate hormone-specific RNA synthesis**.
- This results in the **synthesis of specific proteins** that mediate a number of physiologic functions.

Mechanism of Action

Other pathways have been identified lead to more rapid actions:

- For example, activation of an estrogen receptor in the membranes of hypothalamic cells has been shown to couple to a G protein, thereby initiating a second-messenger cascade.

- In addition, estrogen-mediated dilation of coronary arteries occurs by the increased formation and release of nitric oxide and prostacyclin in endothelial cells.

Classification of Preparations

1. Natural estrogens: Contain a *steroid nucleus*

Estradiol

- is the most potent and the principal estrogen secreted by the ovary.

- metabolized In the liver: to less potent metabolites

- orally have low bioavailability??? undergo first- pass metabolism

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2. Synthetic oestrogens: Orally

Have prolonged action (stored in fat) & higher potency

- **Ethinyl estradiol:**
  Highly potent, taken orally (ethinyl group protects from inactivation).

- **Mestranol: rapidly demethylated to Ethinyl Estradiol.**

- **Estradiol valerate:**
  - **cleaved to estradiol and valeric acid**
  - **Also available as parentral dosage form (I.M)**

- Most estrogens are absorbed from skin and mucous membrane and can be given as transdermal patches.

- Can be given topically in the vagina as pessaries or creams for local effect but some of the drugs can be absorbed.

Pharmacological Actions

1) Uterus:

Responsible for the **proliferative phase** of the cycle on endometrium.

Together **with progesterone for the "secretory phase".**

Estrogens affect the growth of the myometrium &↑sensitivity to oxytocin.

2) Breast:

stimulates growth of the mammary glands (the duct system and nipple).

3) Alterations in composition of plasma lipids:

↓ LDL.

↓ Plasma cholesterol.

↑ HDL

↑ Plasma triglycerides.

4) ↑↑ deposition of Ca++ in bones,

rapid growth of long bones during puberty in females

and acceleration of epiphyseal closure.

5) Blood Coagulation:

estrogens enhance the coagulability of blood.

↑ circulating levels of factors II, VII, IX and X (2,7,9 & 10)

High incidence of thromboembolic disease

Therapeutic uses

1)Contraception: with progestogens.

2)Postmenopausal hormonal therapy(HT)

for menopausal symptoms" hot flushes & vaginal atrophy".

- With intact uterus add progestogen to # risk of endomerial carcinoma.
- Doses of HT are less than that in oral contraception→ less side effects
- Lowest effective doses for the shortest possible time (for risk of side effect)
- If only vaginal atrophy → use vaginal estrogen

3)Replacement therapy (estrogen & progestogen) in:

- **1ry hypogonadism (ovarian failure).**
- **Premature menopause**
- **Surgical menopause**

Adverse effects

1)Nausea and Breast tenderness (most common)

2) Thromboembolic events & myocardial infarction

(contraindicated with history of **Thromboembolism)**

3)Salt & water retention →**edema & hypertension →**
↑↑ weight gain

4) Increased blood sugar levels

5) Risk of **breast cancer.**

6) Risk of **endometrial carcinoma** # by progesterone.

7) Carcinoma of vagina in women whose mother was treated **by estrogen early in pregnancy**

SUGGESTED TEXTBOOKS

1.

2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.


THANK
YOU